Comparison of Estimated PCB-153 Concentrations in Human Milk Using Various Pharmacokinetic Models

Farrer[1], Poulsen[2], Davoli[3], Bailey, Moffett[4], Welsh[4], Yang[4], Haddad[5]

Risk to infants from consuming contaminated human milk has long been overlooked in the risk assessment process. Typically, risk assessors estimate doses of lipophilic contaminants based on their measured concentrations in media of concern. The medium of human milk is often difficult to sample for contaminant concentrations. Therefore, it is desirable to have models that predict contaminant levels in human milk and subsequent average daily doses to the nursing infant (ADDi). Researchers have developed several of these models. The aim of this study was to compare three models in an effort to help risk assessors and public health practitioners choose an appropriate method to estimate risk to infants via the human milk exposure pathway. The three models chosen for comparison were : 1) a classical single-compartment pharmacokinetic model consisting of a mass-transfer algorithm that calculates a maternal body burden from average daily dose, 2) a 3-compartment physiologically-based pharmacokinetic (PBPK) model developed by Redding et al. [ÈHP 2008 116: 1629-1634], and 3) a second PBPK model with 8 compartments developed by Verner et al. [ÈHP 2009 117:481-487]. The models were compared by running two sets of simulations in each model using the polychlorinated biphenyl congener 153 (PCB-153), a widespread lipophilic environmental contaminant relevant to human health. The first set of simulations used a back-calculated ADDm as a starting point. This ADDm was calculated using the 8-compartment PBPK model based on PCB-153 blood concentrations measured in an actual human population. From this derived ADDm, the three models simulated both the milk concentration and ADDi. The estimated milk concentrations were then compared to observed concentrations. The second set of simulations used an ADDm derived for ~~from~~ PCB-153 assuming consumption of contaminated fish. ~~concentrations measured in fish from a contaminated water way and standard fish consumption rates.~~ We then compared the human milk concentrations and ADDi resulting from simulations across the three models. In all cases the classical pharmacokinetic model produced the highest estimates of PCB-153 concentration in human milk and ADDi. Our results will be used to recommend an appropriate ~~suggest that using~~ model for risk assessors and public health practitioners to ~~s~~ to use for predicting the ADDi for lipophilic environmental contaminants. ~~may be a useful tool for risk assessors and public health practitioners in making decisions about environmental clean-up and public health interventions.~~

Commented [h1]: I am not too sure about this conclusion which seems too general and could have been said before even doing this study.

[1] Oregon Department of Human Services
[2] Oregon Department of Environmental Quality
[3] United States Environmental Protection Agency
[4] Agency for Toxic Substances and Disease Registry
[5] Dept. of Biological Sciences, TOXEN, Université du Québec à Montréal